



EDITORIALS

Uncertainty in medicine

Patients, doctors, and the wider public need a better understanding of medicine's limitations

Steven Hatch *associate professor of medicine*

UMass Medical School, Worcester, MA, USA

Uncertainty is ubiquitous in medicine. It can be seen in something as basic as a differential diagnosis or as complex as a new set of guidelines by a professional society. And yet uncertainty is often ignored as a subject in medicine, its importance underappreciated and its consequences suppressed. The public could be forgiven for regarding physicians as trafficking in certitude, producing diagnoses or summarising research with triumphant finality. To a large extent, we participate in that self delusion, and indeed encourage it.

Systematic study

Despite early work,¹ the systematic study of uncertainty did not begin in earnest until the 1990s. Since then, uncertainty has usually been studied in relation to professional development. A 2014 study, for example, reported that certain personality traits of general practitioners influenced their levels of anxiety about uncertainty; the authors note this may lead to resource overuse and medical errors.² Nevertheless, the general lack of attention to uncertainty led to one recent high profile lament that “the culture of medicine evinces a deep rooted unwillingness to acknowledge and embrace it.”³ Decades after the problem was identified, it remains entrenched, and, in an age of ever increasing objective data, it is arguably worse.

Disputes about how to incorporate uncertainty into medical management have contributed to major controversies in the past few years. For example, guidelines on mammography remain contentious, with some organisations advocating an aggressive screening strategy⁴ and others taking the opposite approach,⁵ the differences resting on alternative interpretations of the consequences of false positive results in low prevalence age groups. Similarly, the drafting of the eighth Joint National Committee (JNC 8) guidelines on the management of high blood pressure were so contentious that a dissenting minority group issued a competing set of guidelines.⁶ The dispute was mostly not caused by conflicting analysis about which studies were optimally designed, but rather how forcefully a threshold recommendation should be made given the inherent fuzziness of the data.

Rhetorical and scientific problem

Uncertainty is therefore as much a rhetorical as a scientific problem. Modern, rigorous clinical trial design has yielded more robust data but has also made a fetish of “significance,” where a P value of <0.05 can substitute for a more nuanced understanding of data. A recent paper on adjuvant treatment of breast cancer with aromatase inhibitors shows the problem.⁷ The conclusion of the abstract notes that aromatase inhibitors “resulted in significantly higher rates of disease-free survival,” and then notes, “but the rate of overall survival was not higher.” The “significantly higher” rate the authors tout is a mere 4%, which implies a substantial amount of uncertainty that there will be a tangible benefit for any given patient. Nevertheless, the authors choose to lead with this assertion, adding that the treatment had no effect on mortality as an apparent afterthought. The trial design isn't bad, but the language used to frame the results most certainly is.

Avoiding overconfidence

Failure to acknowledge uncertainty results in overconfidence and inevitably leads to the phenomenon of “medical reversal,” in which well designed trials overturn existing medical practices. Many established practices have become accepted through the advocacy of prominent figures rather than careful study. In a seminal paper, Prasad and colleagues reviewed all original articles in a high impact journal between 2000 and 2010, and found that about 40% of the 363 articles testing the standard of care resulted in medical reversal.⁸ Arguably, the majority of these reversals could have been avoided if the uncertainty inherent in the established practice had been acknowledged and contextualised based on the strength of evidence.

How can we be more forthright about uncertainty and avoid overconfidence? One simple solution could be to add an “uncertainty grade” to abstracts, summarising the quality of evidence as well as the magnitude of the effect. The GRADE approach to evidence already does this for an increasing number of clinical guidelines,⁹ including a recent guideline on opiates for the treatment of chronic pain.¹⁰ The recommendations use GRADE to consider the quality of the overall evidence along

with its clinical context, providing some manoeuvring space for both clinician and patient.

In practice, the admission of uncertainty forms the starting point for a more open conversation between patient and clinician. By being more direct about our limitations, we are likely to foster greater trust and hopefully greater confidence in our joint efforts to manage the patient's condition. We ignore those benefits at our peril.

Competing interests: I have read and understood BMJ policy on declaration of interests and have no relevant interests to declare.

Provenance and peer review: Commissioned; not externally peer reviewed.

- 1 Ledley RS, Lusted LB. Reasoning foundations of medical diagnosis; symbolic logic, probability, and value theory aid our understanding of how physicians reason. *Science* 1959;357:9-21. doi:10.1126/science.130.3366.9 pmid:13668531.
- 2 Schneider A, Wübken M, Linde K, Bühner M. Communicating and dealing with uncertainty in general practice: the association with neuroticism. *PLoS One* 2014;357:e102780. doi:10.1371/journal.pone.0102780 pmid:25029276.

- 3 Simpkin AL, Schwartzstein RM. Tolerating uncertainty: the next medical revolution? *N Engl J Med* 2016;357:1713-5. doi:10.1056/NEJMp1606402 pmid:27806221.
- 4 American College of Obstetricians and Gynecologists. Practice bulletin No 122: breast cancer screening. *Obstet Gynecol* 2011;357:372-82. doi:10.1097/AOG.0b013e31822c98e5 pmid:21775869.
- 5 Nelson H, Cantor A, Humphrey L, Fu R, Pappas M, Daeges M, et al. Screening for breast cancer: a systematic review to update the 2009 US Preventive Services Task Force recommendation. Agency for Healthcare Research and Quality, 2016.
- 6 Peterson ED, Gaziano JM, Greenland P. Recommendations for treating hypertension: what are the right goals and purposes? *JAMA* 2014;357:474-6. doi:10.1001/jama.2013.284430 pmid:24352710.
- 7 Goss PE, Ingle JN, Pritchard KI, et al. Extending aromatase-inhibitor adjuvant therapy to 10 years. *N Engl J Med* 2016;357:209-19. doi:10.1056/NEJMoa1604700 pmid:27264120.
- 8 Prasad V, Vandross A, Toomey C, et al. A decade of reversal: an analysis of 146 contradicted medical practices. *Mayo Clin Proc* 2013;357:790-8. doi:10.1016/j.mayocp.2013.05.012 pmid:23871230.
- 9 Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;357:383-94. doi:10.1016/j.jclinepi.2010.04.026 pmid:21195583.
- 10 Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep* 2016;357:1-49. doi:10.15585/mmwr.r6501e1 pmid:26987082.

Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to <http://group.bmj.com/group/rights-licensing/permissions>